L Number	Hits	Search Text	DB	Time stamp
1	20129	"transcription factor"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:34
2	26550	transcription WITH regulat$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:34
3	7502	(transcription WITH regulat$) SAME "gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:35
4	5092	((transcription WITH regulat$) SAME "gene expression") and "transcription factor"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:35
5	8916	"transcription factor" WITH regulat$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:35
6	43516	DNA WITH binding	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:35
7	6325	("transcription factor" WITH regulat$) and (DNA WITH binding)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:35
8	2652	("transcription factor" WITH regulat$) SAME (DNA WITH binding)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:35
9	371	(("transcription factor" WITH regulat$) SAME (DNA WITH binding)) and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:36
10	45858	("small molecule" or ligand)WITH binding	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:36
11	353	((("transcription factor" WITH regulat$) SAME (DNA WITH binding)) and aptamer) and (("small molecule" or ligand)WITH binding)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:39
12	536	"transcription regulatory" WITH protein	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:40
13	3	((((("transcription factor" WITH regulat$) SAME (DNA WITH binding)) and aptamer) and (("small molecule" or ligand)WITH binding)) and ("transcription regulatory" WITH protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:41
14	13352	inhibit$ WITH translation	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:41
15	306	(((("transcription factor" WITH regulat$) SAME (DNA WITH binding)) and aptamer) and (("small molecule" or ligand)WITH binding)) and (inhibit$ WITH translation)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 16:44
16	54	("transcription regulatory" WITH protein) SAME "gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:05
17	39598	|536/23.1|536/23.4|536/24.1|536/24.5|536/24[illegible]	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:07

18	1178	|536/23.1|536/23.4|536/24.1|536/24.5|536/24 and aptamer	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:08
19	967	(|536/23.1|536/23.4|536/24.1|536/24.5|536/24 and aptamer) and translation	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:08
20	630	((|536/23.1|536/23.4|536/24.1|536/24.5|536/24 and aptamer) and translation) and (transcription WITH regulat$)	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:08
21	578	(((|536/23.1|536/23.4|536/24.1|536/24.5|536/24 and aptamer) and translation) and (transcription WITH regulat$)) and ligand	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:08
22	535	((((|536/23.1|536/23.4|536/24.1|536/24.5|536/24 and aptamer) and translation) and (transcription WITH regulat$)) and ligand) and (DNA WITH binding)	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:09
23	498	((((|536/23.1|536/23.4|536/24.1|536/24.5|536/24 and aptamer) and translation) and (transcription WITH regulat$)) and ligand) and (DNA WITH binding)) and	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:09
24	378	(("small molecule" or ligand) WITH |536/24.5|536/24 binding) and aptamer) and translation) and (transcription WITH regulat$)) and ligand) and (DNA WITH binding)) and	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:09
25	235	(("small molecule" or ligand) WITH |536/24.5|536/24 binding) and aptamer) and translation) and (transcription WITH regulat$) SAME "gene expression") and ligand) and (DNA WITH binding)) and (("small molecule" or ligand)WITH binding)) and ((transcription WITH regulat$) SAME "gene expression")) and ((("transcription factor" WITH regulat$) SAME (DNA WITH binding)) and aptamer)	US-PAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 17:09

L Number	Hits	Search Text	DB	Time stamp
1	351	ramachandra.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 11:43
2	2974	aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 11:43
4	5	ramachandra.in. and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 11:59
5	56877	"gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 11:59
6	231788	translation$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 11:59
7	1126328	activat$ or repress$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:00
8	24219	e2f-1 or gal4 or stat or "Zinc finger"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:00
9	5620	tup1 or sir1 or nep1 or tsf3 or sfI or sf1 or wt1 or e4bp4 or krab or zf5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:01
10	125041	ligand	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:01
11	5	ramachandra.in. and (ramachandra.in. and aptamer)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:01
12	10	ramachandra.in. and "gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:04
13	1712	aptamer and "gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:04
14	1440	(aptamer and "gene expression") and ligand	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:04
15	1274	((aptamer and "gene expression") and ligand) and translation$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:04
16	1237	(((aptamer and "gene expression") and ligand) and translation$) and (activat$ or repress$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:04
17	1210	aptamer SAME ligand	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:05
18	833	(aptamer SAME ligand) and translation$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:05

19	801	(aptamer SAME ligand) and "gene expression"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:05
20	727	((aptamer SAME ligand) and "gene expression") and translation$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:06
21	1231	Hoechst with "33258"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:09
22	47	(Hoechst with "33258") and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:20
23	617	"molecular switch"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:11
24	18	"molecular switch" and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:18
25	31792	transcript$ SAME (activat$ or repress$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:19
26	88	aptamer SAME (transcript$ SAME (activat$ or repress$))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:19
27	592	aptamer and (e2f-1 or gal4 or stat or "Zinc finger")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:20
28	117	aptamer and (tup1 or sir1 or nep1 or tsf3 or sfI or sf1 or wt1 or e4bp4 or krab or zf5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:20
29	1361	aptamer SAME binding	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:21
30	74	(aptamer SAME binding) SAME (transcript$ SAME (activat$ or repress$))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:29
31	2183	TAM.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:22
32	5	TAM.in. and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:22
33	7711	inhibit WITH translation	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:30
34	51	(inhibit WITH translation) SAME aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:39
35	0	choo.in	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:35
36	1707	choo.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:35

37	3	choo.in. and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:35
38	14260	green.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:38
39	8	green.in. and aptamer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/07/29 12:38

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 16:47:01 ON 29 JUL 2004

L1	1201	S	"TRANSCRIPTION FACTOR" (S) MODULATION
L2	158	S	"TRANSCRIPTION REGULATORY PROTEIN"
L3	893163	S	TRANSCRIPTION
L4	45976	S	L3 (S) (ACTIVATOR OR REPRESSOR)
L5	177	S	L1 AND L4
L6	90	S	L5 NOT PY>=2001
L7	60		DUP REM L6 (30 DUPLICATES REMOVED)
L8	3149770	S	DNA OR "NUCLEIC ACID"
L9	4068886	S	RNA OR "NUCLEIC ACID" OR DNA
L10	386041	S	L9 (S) BINDING
L11	28	S	L10 AND L7
L12	28		DUP REM L11 (0 DUPLICATES REMOVED)

```
FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 11:23:46 ON 29 JUL 2004
L1          2396 S APTAMER
L2        219190 S TRANSCRIPTION (S) REGULAT?
L3            21 S L1 (P) L2
L4            15 DUP REM L3 (6 DUPLICATES REMOVED)
L5             6 S L4 NOT PY>=2001
L6       1259336 S TRANSCRIPT?
L7       3213626 S ACTIVAT? OR REPRESS?
L8         68143 S E2F-1 OR GAL4 OR STAT OR "ZINC FINGER"
L9        410882 S L6 AND L7
L10           94 S L9 AND L1
L11           19 S L10 NOT PY>=2001
L12            8 DUP REM L11 (11 DUPLICATES REMOVED)
L13        28720 S L7 (P) L8
L14            8 S L13 AND L1
L15            6 DUP REM L14 (2 DUPLICATES REMOVED)
L16         8251 S TUP1 OR SIR1 OR NEP1 OR TSF3 OR SFI OR WT1 OR E4BP4 OR KRAB O
L17         2359 S L16 (P) L9
L18         2405 S L16 (P) L7
L19            0 S L18 AND L1
L20       827207 S TRANSLAT?
L21           13 S L20 AND L2 AND L1
L22           11 DUP REM L21 (2 DUPLICATES REMOVED)
L23            4 S L22 NOT PY>=2001
L24          711 S L18 AND L2
L25           31 S L24 AND L20
L26           23 S L25 NOT PY>=2001
L27           10 DUP REM L26 (13 DUPLICATES REMOVED)
L28            6 S L1 AND L16
L29            3 DUP REM L28 (3 DUPLICATES REMOVED)
L30            0 S L29 NOT PY>=2001
L31       553752 S LIGAND
L32          388 S L1 (P) L31
L33            4 S L32 AND L2
L34            4 DUP REM L33 (0 DUPLICATES REMOVED)
L35           35 S L32 AND L20
L36           14 DUP REM L35 (21 DUPLICATES REMOVED)
L37           10 S RAMACHANDRA/AU
```

NSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:162709 CAPLUS
DOCUMENT NUMBER: 140:176347
TITLE: Aptamer-mediated regulation of gene expression by inhibition of post-transcriptional events
INVENTOR(S): Ramachandra, Murali
PATENT ASSIGNEE(S): Ranji, Inc, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004016638	A1	20040226	WO 2002-US9950	20020319

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2002-US9950 20020319
AB This invention provide a **ligand**-mediated method of regulating gene expression by inhibition of post-transcriptional events. An **aptamer** is positioned in a nucleic acid mol. along with a sequence encoding a transcriptional regulatory polypeptide. The **aptamer** disrupts **translation** of the transcriptional regulatory polypeptide when contacted with an **aptamer**-binding **ligand**. Gene expression levels can be either increased or decreased by the disclosed methods, depending on whether the transcriptional regulatory polypeptide is a repressor or activator, and the degree of the effect is dependent upon the dose of the **ligand** . Nucleic acid mols., expression cassettes, expression vectors and cells useful in the gene regulation methods are also provided.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 2 OF 14 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004115153 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15004248
TITLE: A theophylline responsive riboswitch based on helix slipping controls gene expression in vivo.
AUTHOR: Suess Beatrix; Fink Barbara; Berens Christian; Stentz Regis; Hillen Wolfgang
CORPORATE SOURCE: Lehrstuhl fur Mikrobiologie, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Staudtstrasse 5, 91058 Erlangen, Germany.. bsuess@biologie.uni-erlangen.de
SOURCE: Nucleic acids research, (2004) 32 (4) 1610-4.
Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040310
Last Updated on STN: 20040609
Entered Medline: 20040608
AB Riboswitches are newly discovered regulatory elements which control a wide

set of basic metabolic pathways. They consist solely of RNA, sense their **ligand** in a preformed binding pocket and perform a conformational switch in response to **ligand** binding resulting in altered gene expression. We have utilized the enormous potential of RNA for molecular sensing and conformational changes to develop novel molecular switches with predetermined structural transitions in response to the binding of a small molecule. To validate these in vivo, we exploit the distance-dependent inhibitory potential of secondary structure elements placed close to the bacterial ribosome binding site. We created a **translational** control element by combining the theophylline **aptamer** with a helical communication module for which a **ligand**-dependent one-nucleotide slipping mechanism had been proposed. This structural element was inserted at a position just interfering with **translation** in the non **ligand**-bound form. Addition of the **ligand** then shifts the inhibitory element to a distance which permits efficient **translation**. We present here a novel regulatory mechanism in the first rationally designed, in vivo active RNA switch. Its use of a slippage mechanism to control gene expression makes it different from natural riboswitches which are based on sequestration or antitermination.

L36 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:576917 CAPLUS
TITLE: DNA display. II. Genetic manipulation of combinatorial chemistry libraries for small-molecule evolution
AUTHOR(S): Halpin, David R.; Harbury, Pehr B.
CORPORATE SOURCE: Department of Biochemistry, Stanford University School of Medicine, Stanford, CA, USA
SOURCE: PLoS Biology (2004), 2(7), 1022-1030
CODEN: PBLIBG; ISSN: 1545-7885
URL: http://www.plosbiology.org/archive/1545-7885/2/7/pdf/10.1371_1545-7885_2_7_complete.pdf
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Biol. in vitro selection techniques, such as RNA **aptamer** methods and mRNA display, have proven to be powerful approaches for engineering mols. with novel functions. These techniques are based on iterative amplification of biopolymer libraries, interposed by selection for a desired functional property. Rare, promising compds. are enriched over multiple generations of a constantly replicating mol. population, and subsequently identified. The restriction of such methods to DNA, RNA, and polypeptides precludes their use for small-mol. discovery. To overcome this limitation, we have directed the synthesis of combinatorial chemical libraries with DNA "genes," making possible iterative amplification of a nonbiol. mol. species. By differential hybridization during the course of a traditional split-and-pool combinatorial synthesis, the DNA sequence of each gene is read out and **translated** into a unique small-mol. structure. This "chemical **translation**" provides practical access to synthetic compound populations 1 million-fold more complex than state-of-the-art combinatorial libraries. We carried out an in vitro selection experiment (iterated chemical **translation**, selection, and amplification) on a library of 106 nonnatural peptides. The library converged over three generations to a high-affinity protein **ligand** . The ability to genetically encode diverse classes of synthetic transformations enables the in vitro selection and potential evolution of an essentially limitless collection of compound families, opening new avenues to drug discovery, catalyst design, and the development of a materials science "biol.".

L36 ANSWER 4 OF 14 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004309031 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15210347

TITLE: DNA helix-stack switching as the basis for the design of versatile deoxyribosensors.
AUTHOR: Sankar Carlo G; Sen Dipankar
CORPORATE SOURCE: Department of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, BC, Canada V5A 1S6.
SOURCE: Journal of molecular biology, (2004 Jul 9) 340 (3) 459-67. Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040624
Last Updated on STN: 20040716

AB The charge conduction properties of DNA can be harnessed for monitoring the binding of a **ligand** to its receptor. Two classes of such DNA-based sensors (deoxyribosensors) have been described for the **ligand** adenosine, each generated by the functional coupling of an adenosine-specific DNA **aptamer** to a charge-conductive DNA path. Here, we report a systematic investigation of the extent to which the features of such **ligand**-specific deoxyribosensors can be made universal. We have exploited established rules for DNA helical stacking within three-way helical junctions to design and characterize the properties of deoxyribosensors specific for the amino acid derivative, argininamide. The biochemical detection methods described here should **translate** easily to direct and rapid measurements of changes in current flow using chip-based methods. The results presented here suggest general directions for the design and assembly of deoxyribosensors specific for any molecular **ligand**, and describe a novel methodology for investigating helical stacking within DNAs and RNAs of unknown tertiary folding, such as novel ribozymes and deoxyribozymes. Copyright 2004 Elsevier Ltd.

L36 ANSWER 5 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2004349142 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15221028
TITLE: DNA Display II. Genetic Manipulation of Combinatorial Chemistry Libraries for Small-Molecule Evolution.
AUTHOR: Halpin David R; Harbury Pehr B
CORPORATE SOURCE: Department of Biochemistry, Stanford University School of Medicine, Stanford, California, United States of America.
SOURCE: PLoS biology, (2004 Jul) 2 (7) E174. Journal code: 101183755. ISSN: 1544-9173.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040715
Last Updated on STN: 20040715

AB Biological in vitro selection techniques, such as RNA **aptamer** methods and mRNA display, have proven to be powerful approaches for engineering molecules with novel functions. These techniques are based on iterative amplification of biopolymer libraries, interposed by selection for a desired functional property. Rare, promising compounds are enriched over multiple generations of a constantly replicating molecular population, and subsequently identified. The restriction of such methods to DNA, RNA, and polypeptides precludes their use for small-molecule discovery. To overcome this limitation, we have directed the synthesis of combinatorial chemistry libraries with DNA "genes," making possible iterative amplification of a nonbiological molecular species. By differential hybridization during the course of a traditional split-and-pool combinatorial synthesis, the DNA sequence of each gene is read out and **translated** into a unique small-molecule structure. This "chemical **translation**" provides practical access to

synthetic compound populations 1 million-fold more complex than state-of-the-art combinatorial libraries. We carried out an in vitro selection experiment (iterated chemical **translation**, selection, and amplification) on a library of 10(6) nonnatural peptides. The library converged over three generations to a high-affinity protein **ligand**. The ability to genetically encode diverse classes of synthetic transformations enables the in vitro selection and potential evolution of an essentially limitless collection of compound families, opening new avenues to drug discovery, catalyst design, and the development of a materials science "biology."

L36 ANSWER 6 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2003448190 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14500841
TITLE: Selective inhibitory DNA aptamers of the human RNase H1.
AUTHOR: Pileur Frederic; Andreola Marie-Line; Dausse Eric; Michel Justine; Moreau Serge; Yamada Hirofumi; Gaidamakov Sergei A; Crouch Robert J; Toulme Jean-Jacques; Cazenave Christian
CORPORATE SOURCE: INSERM U386, IFR Pathologies Infectieuses, Universite Victor Segalen Bordeaux 2, 146, rue Leo Saignat, 33076 Bordeaux cedex, France.
SOURCE: Nucleic acids research, (2003 Oct 1) 31 (19) 5776-88. Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030928
Last Updated on STN: 20031021
Entered Medline: 20031020

AB Human RNase H1 binds double-stranded RNA via its N-terminal domain and RNA-DNA hybrid via its C-terminal RNase H domain, the latter being closely related to Escherichia coli RNase HI. Using SELEX, we have generated a set of DNA sequences that can bind efficiently (K(d) values ranging from 10 to 80 nM) to the human RNase H1. None of them could fold into a simple perfect double-stranded DNA hairpin confirming that double-stranded DNA does not constitute a trivial **ligand** for the enzyme. Only two of the 37 DNA aptamers selected were inhibitors of human RNase H1 activity. The two inhibitory oligomers, V-2 and VI-2, were quite different in structure with V-2 folding into a large, imperfect but stable hairpin loop. The VI-2 structure consists of a central region unimolecular quadruplex formed by stacking of two guanine quartets flanked by the 5' and 3' tails that form a stem of six base pairs. Base pairing between the 5' and 3' tails appears crucial for conferring the inhibitory properties to the **aptamer**. Finally, the inhibitory aptamers were capable of completely abolishing the action of an antisense oligonucleotide in a rabbit reticulocyte lysate supplemented with human RNase H1, with IC50 ranging from 50 to 100 nM.

L36 ANSWER 7 OF 14 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003140233 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12655001
TITLE: Conditional gene expression by controlling **translation** with tetracycline-binding aptamers.
AUTHOR: Suess Beatrix; Hanson Shane; Berens Christian; Fink Barbara; Schroeder Renee; Hillen Wolfgang
CORPORATE SOURCE: Lehrstuhl fur Mikrobiologie, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Staudtstrasse 5, 91058 Erlangen, Germany.. bsuess@biologie.uni-erlangen.de
SOURCE: Nucleic acids research, (2003 Apr 1) 31 (7) 1853-8. Journal code: 0411011. ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030326
Last Updated on STN: 20030417
Entered Medline: 20030416

AB We present a conditional gene expression system in Saccharomyces cerevisiae which exploits direct RNA-metabolite interactions as a mechanism of genetic control. We inserted preselected tetracycline (tc) binding aptamers into the 5'-UTR of a GFP encoding mRNA. While **aptamer** insertion generally reduces GFP expression, one group of aptamers displayed an additional, up to 6-fold, decrease in fluorescence upon tc addition. Regulation is observed for aptamers inserted cap-proximal or near the start codon, but is more pronounced from the latter position. Increasing the thermodynamic stability of the **aptamer** augments regulation but reduces expression of GFP. Decreasing the stability leads to the opposite effect. We defined nucleotides which influence the regulatory properties of the **aptamer**. Exchanging a nucleotide probably involved in tc binding only influences regulation, while mutations at another position alter expression in the absence of tc, without affecting regulation. Thus, we have developed and characterized a regulatory system which is easy to establish and controlled by a non-toxic, small **ligand** with good cell permeability.

L36 ANSWER 8 OF 14 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003454847 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12950926
TITLE: Tetracycline-aptamer-mediated **translational** regulation in yeast.
AUTHOR: Hanson Shane; Berthelot Karine; Fink Barbara; McCarthy John E G; Suess Beatrix
CORPORATE SOURCE: Lehrstuhl fur Mikrobiologie, Friedrich-Alexander Universitat Erlangen-Nurnberg, Staudtstrasse 5, 91058 Erlangen, Germany.
SOURCE: Molecular microbiology, (2003 Sep) 49 (6) 1627-37. Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031001
Last Updated on STN: 20031218
Entered Medline: 20031211

AB We describe post-transcriptional gene regulation in yeast based on direct RNA-**ligand** interaction. Tetracycline-dependent **translational** regulation could be imposed via specific aptamers inserted at two different positions in the 5' untranslated region (5'UTR). **Translation** in vivo was suppressed up to ninefold upon addition of tetracycline. Repression via an **aptamer** located near the start codon (cap-distal) in the 5'UTR was more effective than repression via a cap-proximal position. On the other hand, suppression in a cell-free system reached maximally 50-fold and was most effective via a cap-proximal **aptamer**. Examination of the kinetics of tetracycline-dependent **translational** inhibition in vitro revealed that preincubation of tetracycline and mRNA before starting **translation** led not only to the fastest onset of inhibition but also the most effective repression. The differences between the behaviour of the regulatory system in vivo and in vitro are likely to be related to distinct properties of mRNP structure and mRNA accessibility in intact cells as opposed to cell-extracts. Tetracycline-dependent regulation was also observed after insertion of an

uORF sequence upstream of the **aptamer**, indicating that our system also targets reinitiating ribosomes. Polysomal gradient analyses provided insight into the mechanism of regulation. Cap-proximal insertion inhibits binding of the 43S complex to the cap structure whereas start-codon-proximal aptamers interfere with formation of the 80S ribosome, probably by blocking the scanning preinitiation complex.

L36 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:615782 CAPLUS
DOCUMENT NUMBER: 137:151148
TITLE: Post-transcriptional regulation of expression of a constitutively transcribed gene at **translational** level by binding of a **ligand** to an **aptamer** domain in the transcript
INVENTOR(S): Ramachandra, Murali
PATENT ASSIGNEE(S): Canji, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062949	A2	20020815	WO 2001-US50722	20011019
WO 2002062949	A3	20021031		
WO 2002062949	C2	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002115629	A1	20020822	US 2001-36091	20011019
EP 1410021	A2	20040421	EP 2001-270163	20011019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: US 2000-242106P P 20001020
WO 2001-US50722 W 20011019

AB This invention provide a **ligand**-mediated method of regulating gene expression by inhibition of post-transcriptional events. The gene encodes a transcription factor and includes an **aptamer** in the transcript. The gene is expressed from a constitutive promoter. The **aptamer** disrupts **translation** of the transcriptional regulatory polypeptide when contacted with its **ligand**. Gene expression levels can be either increased or decreased, depending on whether the transcription factor is a repressor or activator, and the degree of the effect is dependent upon the dose of the **ligand**. Nucleic acid mols., expression cassettes, expression vectors and cells useful in the gene regulation methods are also provided.

L36 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:352829 CAPLUS
DOCUMENT NUMBER: 137:74882
TITLE: Inhibition of **translation** by RNA-small molecule interactions
AUTHOR(S): Harvey, Isabelle; Garneau, Philippe; Pelletier, Jerry
CORPORATE SOURCE: Department of Biochemistry, McIntyre Medical Sciences,

McGill University, Montreal, QC, H3G 1Y6, Can.
SOURCE: RNA (2002), 8(4), 452-463
CODEN: RNARFU; ISSN: 1355-8382
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Small mol. ligand-RNA interactions have the potential to influence gene expression at a variety of steps and in a number of ways. Here, we demonstrate that such interactions are sufficiently stable to inhibit **translation** of eukaryotic mRNAs in vitro and in vivo. Inhibition is only observed when the 5' UTR of the mRNA is targeted, and the response is proportional to the number of binding sites within this region. We find that small mol. ligand-RNA interactions can be sufficiently stable to prevent 80S ribosome assembly on an mRNA template. The ability to specifically ablate expression of a defined mRNA with a small mol. ligand demonstrates proof of principle for pharmacol. targeting aimed at controlling **translation** of specific mRNAs.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 11 OF 14 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001509812 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11557344
TITLE: Inducible regulation of the S. cerevisiae cell cycle mediated by an RNA **aptamer-ligand** complex.
AUTHOR: Grate D; Wilson C
CORPORATE SOURCE: Department of Biology and Center for the Molecular Biology of RNA, University of California at Santa Cruz, 95064, USA.
SOURCE: Bioorganic & medicinal chemistry, (2001 Oct) 9 (10) 2565-70.
Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200111
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20011105
Entered Medline: 20011101
AB Previous studies have shown that the introduction of a **ligand** -binding RNA (**aptamer**) into the 5'-UTR of an mRNA can confer regulated expression of both prokaryotic and eukaryotic reporter genes. The current report shows that **aptamer** insertion into the 5'-UTR of a cyclin transcript in S. cerevisiae renders cell-cycle control dependent upon the presence or absence of the target **ligand**. A malachite green binding motif, defined by an asymmetric internal loop flanked by short RNA helices, was inserted immediately upstream of the CLB2 start codon. Progression through the cell cycle is dramatically slowed and elongated bud morphology develops when tetramethylrosamine (a fluorescent malachite green analogue) is added to the **aptamer** -containing strain. Quantification of CLB2 expression at the RNA and protein levels by RT-PCR and Western blot analysis, respectively, demonstrates that the **aptamer ligand** regulates transcript **translatability** rather than stability. One-dimensional NMR spectroscopy shows that the malachite green binding **aptamer** undergoes a dramatic **ligand**-dependent change in structure with many nucleotides folding to adopt a well-defined conformation. These results are consistent with a model in which **translational** initiation is blocked by **ligand**-induced conformational changes in the 5'-UTR.

L36 ANSWER 12 OF 14 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2001150052 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11162119
TITLE: Probing the kinetics of formation of the bacteriophage MS2 **translational** operator complex: identification of a protein conformer unable to bind RNA.
AUTHOR: Lago H; Parrott A M; Moss T; Stonehouse N J; Stockley P G
CORPORATE SOURCE: Astbury Centre for Structural Molecular Biology, Faculty of Biological Sciences, University of Leeds, Leeds, LS2 9JT, UK.
SOURCE: Journal of molecular biology, (2001 Feb 2) 305 (5) 1131-44.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010315

AB We have investigated the kinetics of complex formation between bacteriophage MS2 coat protein subunits and synthetic RNA fragments encompassing the natural **translational** operator site, or the consensus sequences of three distinct RNA **aptamer** families, which are known to bind to the same site on the protein. Reactions were assayed using stopped-flow fluorescence spectroscopy and either the intrinsic tryptophan fluorescence of the protein or the signals from RNA fragments site-specifically substituted with the fluorescent adenosine analogue 2'-deoxy, 2-aminopurine. The kinetics observed were independent of the fluorophore being monitored or its position within the complex, indicating that the data report global events occurring during complex formation. Competition assays show that the complex being formed consists of a single coat protein dimer and one RNA molecule. The binding reaction is at least biphasic. The faster phase, constituting 80-85 % of the amplitude, is a largely diffusion driven RNA-protein interaction (k1 approximately 2x10(9) M(-1) s(-1)). The salt dependence of the forward reaction and the similarities of the on-rates of lower-affinity RNA fragments are consistent with a diffusion-controlled step dominated by electrostatic steering. The slower phase is independent of reactant concentration, and appears to correspond to isomerisation of the coat protein subunit(s) prior to RNA binding (k(iso) approximately 0.23 s(-1)). Measurements with a coat protein mutant (Pro78Asn) show that this phase is not due to cis-trans isomerisation at this residue. The conformational changes in the protein **ligand** during formation of an RNA-protein complex might play a role in the triggering of capsid self-assembly and a model for this is discussed.

L36 ANSWER 13 OF 14 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000138235 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10671531
TITLE: In vitro selection of RNA molecules that inhibit the activity of ricin A-chain.
AUTHOR: Hesselberth J R; Miller D; Robertus J; Ellington A D
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of Texas, Austin, Texas 78712, USA.
SOURCE: Journal of biological chemistry, (2000 Feb 18) 275 (7) 4937-42.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330

Preserves protein translation i.e. ribosome assembly

Last Updated on STN: 20000330
Entered Medline: 20000321

AB The cytotoxin ricin disables **translation** by depurinating a conserved site in eukaryotic rRNA. In vitro selection has been used to generate RNA ligands (aptamers) specific for the catalytic ricin A-chain (RTA). The anti-RTA aptamers bear no resemblance to the normal RTA substrate, the sarcin-ricin loop (SRL), and were not depurinated by RTA. An initial 80-nucleotide RNA **ligand** was minimized to a 31-nucleotide **aptamer** that contained all sequences and structures necessary for interacting with RTA. This minimal RNA formed high affinity complexes with RTA (K(d) = 7.3 nM) which could compete directly with the SRL for binding to RTA. The **aptamer** inhibited RTA depurination of the SRL and could partially protect **translation** from RTA inhibition. The IC(50) of the **aptamer** for RTA in an in vitro **translation** assay is 100 nM, roughly 3 orders of magnitude lower than a small molecule inhibitor of ricin, pteroic acid, and 2 orders of magnitude lower than the best known RNA inhibitor. The novel anti-RTA aptamers may find application as diagnostic reagents for a potential biological warfare agent and hold promise as scaffolds for the development of strong ricin inhibitors.

L36 ANSWER 14 OF 14 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1998438700 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9765156
TITLE: Controlling gene expression in living cells through small molecule-RNA interactions.
AUTHOR: Werstuck G; Green M R
CORPORATE SOURCE: Howard Hughes Medical Institute, Program in Molecular Medicine, University of Massachusetts Medical Center, 373 Plantation Street, Suite 309, Worcester, MA 01605, USA.
SOURCE: Science, (1998 Oct 9) 282 (5387) 296-8.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981026

AB Short RNA aptamers that specifically bind to a wide variety of ligands in vitro can be isolated from randomized pools of RNA. Here it is shown that small molecule aptamers also bound their **ligand** in vivo, enabling development of a method for controlling gene expression in living cells. Insertion of a small molecule **aptamer** into the 5' untranslated region of a messenger RNA allowed its **translation** to be repressible by **ligand** addition in vitro as well as in mammalian cells. The ability of small molecules to control expression of specific genes could facilitate studies in many areas of biology and medicine.

' ANSWER 1 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:278857 BIOSIS
DOCUMENT NUMBER: PREV200000278857
TITLE: Specific gene activation by chimeric **Gal4** transcription factors in stable transgenic plants.
AUTHOR(S): Liu, Zhan-Bin [Inventor, Reprint author]; Odell, Joan Tellefsen [Inventor]
CORPORATE SOURCE: Unionville, PA, USA
ASSIGNEE: E. I. du Pont de Nemours and Company, Wilmington, DE, USA
PATENT INFORMATION: US 5968793 October 19, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 19, 1999) Vol. 1227, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jul 2000
Last Updated on STN: 7 Jan 2002

AB A method for **regulating gene expression** in a stably transformed transgenic plant cell utilizing a **Gal4** chimeric **transcription factor** is described.

L9 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1998252810 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9584119
TITLE: Spatial and temporal targeting of gene expression in Drosophila by means of a tetracycline-dependent transactivator system.
AUTHOR: Bello B; Resendez-Perez D; Gehring W J
CORPORATE SOURCE: Biozentrum, University of Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland.. bbello@nimr.mrc.ac.uk
SOURCE: Development (Cambridge, England), (1998 Jun) 125 (12) 2193-202.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980811
Last Updated on STN: 19980811
Entered Medline: 19980730

AB In order to evaluate the efficiency of the tetracycline-regulated gene expression system in Drosophila, we have generated transgenic lines expressing a tetracycline-controlled transactivator protein (tTA), with specific expression patterns during embryonic and larval development. These lines were used to direct expression of a tTA-responsive promoter fused to the coding region of either the beta-galactosidase or the homeotic protein Antennapedia (ANTP), under various conditions of tetracycline treatment. We found that expression of beta-galactosidase can be efficiently inhibited in embryos and larvae with tetracycline provided in the food, and that a simple removal of the larvae from tetracycline exposure results in the induction of the enzyme in a time- and concentration-dependent manner. Similar treatments can be used to prevent the lethality associated with the ectopic expression of ANTP in embryos and, subsequently, to control the timing of expression of the homeoprotein ANTP specifically in the antennal imaginal disc. Our results show that the expression of a gene placed under the control of a tetracycline-responsive promoter can be tightly controlled, both spatially by the regulatory sequences driving the expression of tTA and temporally by tetracycline. This provides the basis of a versatile binary system for **controlling gene expression** in Drosophila, with an additional level of regulation as compared to the general method

using the yeast **transcription factor GAL4**.

L9 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1998412463 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9741432
TITLE: **Tetracycline repressor**, tetR, rather than the tetR-mammalian cell transcription factor fusion derivatives, regulates inducible gene expression in mammalian cells.
AUTHOR: Yao F; Svensjo T; Winkler T; Lu M; Eriksson C; Eriksson E
CORPORATE SOURCE: Division of Plastic Surgery, Brigham and Women's Hospital, Boston, MA 02115, USA.
CONTRACT NUMBER: RO1GM5144904 (NIGMS)
SOURCE: Human gene therapy, (1998 Sep 1) 9 (13) 1939-50.
Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981118

RB155.3 H85

AB This article describes the first (to our knowledge) tetracycline-inducible regulatory system that demonstrates that the **tetracycline repressor** (tetR) alone, rather than tetR-mammalian cell **transcription factor** fusion derivatives, can function as a potent trans-modulator to regulate gene expression in mammalian cells. With proper positioning of tetracycline operators downstream of the TATA element and of human epidermal growth factor (hEGF) as a reporter, we show that gene expression from the tetracycline operator-bearing hCMV major immediate-early enhancer-promoter (pcmvtetO) can be regulated by tetR over three orders of magnitude in response to tetracycline when (1) the reporter was cotransfected with tetR-expressing plasmid in transient expression assays, and (2) the reporter unit was stably integrated into the chromosome of a tetR-expressing cell line. This level of tetR-mediated inducible gene regulation is significantly higher than that of other repression-based mammalian cell transcription switch systems. In an in vivo porcine wound model, close to 60-fold tetR-mediated regulatory effects were detected and it was reversed when tetracycline was administered. Collectively, this study provides a direct implementation of this tetracycline-inducible regulatory switch for **controlling gene expression** in vitro, in vivo, and in gene therapy.

L9 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1998432935 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9758708
TITLE: A novel alternative spliced variant of the transcription factor AP2alpha is expressed in the murine ocular lens.
AUTHOR: Ohtaka-Maruyama C; Hanaoka F; Chepelinsky A B
CORPORATE SOURCE: Cellular Physiology Laboratory, the Institute for Chemical and Physical Science (RIKEN), 2-1 Hirosawa, Wako, Saitama, 351-01, Japan.
SOURCE: Developmental biology, (1998 Oct 1) 202 (1) 125-35.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981028

AB The AP2alpha gene encodes a **transcription factor** containing a basic, helix-span-helix DNA-binding/dimerization domain, which is developmentally regulated and **retinoic acid** inducible. Recent reports about AP2alpha null mice indicate that AP2alpha plays an important role in embryogenesis, especially in craniofacial development and midline fusion. Ocular development is also affected in these null mice. As AP2alpha may be involved in transcriptional regulation in the lens, it was important to examine the expression of the AP2alpha gene in the lens. Four AP2alpha mRNA variants have been previously isolated from whole mouse embryos. Variants 1, 3, and 4 are transcriptional activators that are transcribed from different promoters and variant 2 is a repressor lacking the activation domain encoded by exon 2. Using in situ-PCR, we found that AP2alpha is expressed in the lens epithelia but not in the lens fibers. RT-PCR analysis of lens mRNA with amplimers specific for each variant revealed that AP2alpha variants 1, 2, and 3 are expressed in newborn mouse lenses. However, variant 4 is not expressed in the lens. In this report we characterized a novel isoform, which we named variant 5, expressed in the lens and kidney. Variant 5, which is generated by alternative splicing, may function as a repressor due to the partial deletion of the proline-rich transactivation domain encoded by exon 2. This is the first molecular characterization of AP2alpha gene expression in the lens. Our results indicate that two activator and two repressor AP2alpha isoforms may play a role in **regulating gene expression** in the lens.

L9 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 96148163 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8585942
TITLE: A role for **STAT** family transcription factors in myeloid differentiation.
AUTHOR: Barahmand-pour F; Meinke A; Kieslinger M; Eilers A; Decker T
CORPORATE SOURCE: Vienna Biocenter, Institute of Microbiology and Genetics, Austria.
SOURCE: Current topics in microbiology and immunology, (1996) 211 121-8. Ref: 25
Journal code: 0110513. ISSN: 0070-217X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960404
Last Updated on STN: 19960404
Entered Medline: 19960322

AB **STAT** family transcription factors regulate gene expression in response to a wide variety of cytokines. A **transcription factor** designated differentiation-induced factor (DIF), activated by treatment of myeloid cells with the differentiating agents interferon-gamma (IFN-gamma), granulocyte-macrophage colony-stimulating factor (GM-CSF), colony-stimulating factor-1 (CSF-1) or during phorbol ester-induced differentiation, was characterized as a 112kDa protein related to, but not identical with known isoforms of **STAT** 5. Taken together with previously published results, our data suggest an important function for members of the **STAT** 5 subfamily in **regulating gene expression** during the process of myeloid differentiation.

L9 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 94366732 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7916146
TITLE: c-ErbA, but not **v-ErbA**, competes with a putative erythroid repressor for binding to the carbonic anhydrase II promoter.
AUTHOR: Rascle A; Ghysdael J; Samarut J
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire et Cellulaire, CNRS UMR49, INRA, Ecole Normale Superieure de Lyon, France.
SOURCE: Oncogene, (1994 Oct) 9 (10) 2853-67.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 19970203
Entered Medline: 19941013

AB The carbonic anhydrase II (CAII) gene is the only known gene identified as direct target for **v-ErbA**-mediated repression in avian erythroleukemic cells transformed by Avian Erythroblastosis Virus (AEV). This gene is transcriptionally activated by thyroid hormone (T3) in normal erythrocytic cells. In this work we have analysed the molecular basis of the transcriptional control of the CAII gene by c-ErbA and **v-ErbA**. We show that several domains in the promoter control hormonal regulation of transcription. One domain proximal to the TATA box mediates T3 response but contains no identified binding site for c-ErbA. An other domain termed PAL2 is approximately 600 bp upstream the transcription initiation site and contains a c-ErbA binding site. We show that when it is associated to a heterologous promoter this site mediates transcriptional repression in erythrocytic cells but not in HeLa cells. Moreover, this site binds a nuclear erythrocyte-specific factor that we called NFX, which is different from c-ErbA. heterodimers between c-ErbA and the 9-cis **retinoic acid** receptor (RXR) compete with NFX for binding to PAL2. In contrast, **v-ErbA** alone or in association with RXR is a very poor competitor and is unable to chase NFX out of the PAL2 site. We propose that NFX is a **transcription repressor** whose activity is inhibited by c-ErbA but not **v-ErbA**. This mechanism might contribute to the overall regulation of the carbonic anhydrase II promoter. These data illustrate another possible mechanism through which **v-ErbA** might antagonize the function of c-ErbA in **controlling gene expression**.

RC268.42.D43

11(7):1299-307 p53

~~19(24) p.2619-2627~~

9(10):2853-67 1994 Oct

v-ErbA

PALM INTRANET

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